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CRANE 1623
SN **09/039,260** 03/16/98
Aberg et al.

- Compositions of Descarboethoxyloratadine
- Before the Board of Appeals

Max Bachrach
For Appellant

Examiner's Answer

This is in response to Appellant's brief on appeal filed August 15, 2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims.

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final.

The Appellant's statement of the status of amendments after final rejection contained in the brief is correct in part. As promised examiner has entered amendments to claims **50, 60-61 and 65** as per the amendment filed April 4, 2001, and has also entered the amendment to claim **60** filed with the instant brief. The proposed amendment to claim **54** also filed with the instant brief was not entered because said amendment did not alter in any way the noted claim as presented in the amendment of June 11, 2000.

(5) Summary of Invention.

The summary of invention contained in the brief is deficient

because, following the first seven lines, it describes additional details which are unnecessary to understand the entire scope of the claimed invention.

(6) Issues.

The Appellant's statement of the issues in the brief is substantially correct. The changes are as follows: the text following the term "maintain" at line 3, and "maintained" at lines 8 and 14, are superfluous because what follows each noted term is an argument, not a statement of the issue.

(7) Grouping of Claims.

The appellant's statement in the brief that certain claims do not stand or fall together is not agreed with because Appellant's Groups **I, II, III** and **IV** are directed to overlapping subject matters which are not patentably distinguishable in light of the prior art cited in the art rejections of record. Examiner proposes the following groupings of claims which should stand or fall together.

Examiner's Group **I**: Pharmaceutical compositions of DCL + a decongestant;

Examiner's Group **II**: Pharmaceutical compositions of DCL + other therapeutic agents; and

Examiner's Group **I** encompasses claims **48, 50, 52-54 and 63-65**, and multiply dependent linking claim **61**;

Examiner's Group **II** encompasses claims **55-60 and 66-67**, and multiply dependent linking claim **61**; and

Linking claim: multiply dependent claim **61** links Examiner's Groups **I** and **II**.

(8) Claims Appealed.

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record.

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

Berkow et al. (eds.), The Merck Manual of Diagnosis and Therapy, 16th Edition, Merck Research Laboratories, Rahway, NJ, May, 1992, only pp. 326-332 and 2345-2346 supplied.

Gennaro et al. (eds.), Remington's Pharmaceutical Sciences, 18th Edition, Mack Publishing Co., Easton, PA, 1990, only pp. 1097-1131 (Chs. 58-59) supplied.

Number	Name	Date
4,659,716	**VILLANI**	04/21/87

(10) Grounds of Rejection.

The following grounds of rejection are applicable to the appealed claims:

(10.1) Grounds of Rejection; Anticipation.

The following is a quotation of the appropriate paragraphs of 35

U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

Claims **48, 50, 52-54, 61 and 63-65** are rejected under 35 U.S.C. §102(**b**) as being anticipated by **Villani et al. '716** (PTO-1449 ref. **AC**) wherein **Berkow et al.** (PTO-892 ref. **R**) is only cited to provide the definition of a specific compound well known in the art to be a "decongestant" commonly used in binary pharmaceutical compositions in combination with an antihistamine.

In the Villani et al. reference at column 8, lines 42-46, the combination of DCL and an decongestant in a single pharmaceutical composition is generically taught. The Berkow reference discloses at p. 326 under the heading "Treatment," lines 1-6, in particular lines 4-6, the combination of an antihistamine with the decongestant "pseudoephedrine" in a single pharmaceutical composition. This teaching represents no more than an exemplification of the generic "antihistamine + decongestant" teaching in the Villani reference.

(10.2) Grounds of Rejection; Obviousness.

The following is a quotation of 35 U.S.C. §103(**a**) which forms the basis for all obviousness rejections set forth in this Office action:

"A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the

> subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made."

Claims **48, 50, 52-54, 60-61 and 63-65** are rejected under 35 U.S.C. §103(a) as being unpatentable over **Villani et al. '716** (PTO-1449 ref. **AC**) in view of **Berkow et al.** (PTO-892 ref. **R**).

Villani et al. discloses at column 8, lines 42-46, the combination of DCL and an decongestant in a single pharmaceutical composition is generically taught. This reference does not disclose pharmaceutical compositions wherein the specific decongestant has been specified.

Berkow et al. discloses at p. 326 under the heading "Treatment," lines 1-6, in particular lines 4-6, the combination of an antihistamine with the decongestant "pseudoephedrine" in a single pharmaceutical composition. This reference does not disclose pharmaceutical compositions wherein DCL and any one decongestant have been specified as the active ingredients.

The noted teaching of the Villani reference clearly motivates the ordinary practitioner to go out and find a decongestant to combine with DCL in a binary pharmaceutical composition. For this reason the instant claims are deemed to lack patentable distinction in view of the noted prior art references which do all but teach the specific combination active ingredients specified in claim **54**.

Therefore, the instant claimed binary pharmaceutical compositions comprising DCL and a decongestant, pseudoephedrine in particular, would have been obvious to one of ordinary skill in the art having the above cited references before him at the time the invention was made.

(10.3) Grounds of Rejection; Obviousness.

Claims **55-61 and 66-68** are rejected under 35 U.S.C. §103(a) as being unpatentable over **Villani et al. '716** (PTO-1449 reference **AC**) in view of **Gennaro et al.** (PTO-892 reference **S**).

The instant claims are directed to pharmaceutical compositions comprising DCL and an analgesic selected from the group consisting of acetylsalicylic acid, acetaminophen, ibuprofen, ketoprofen and naproxen.

The Villani et al. reference at column 8, lines 42-46, the combination of DCL and "other therapeutic agents" in a single pharmaceutical composition of the kind found in claims ***5-8***, particularly claim ***5*** which is directed to "an antihistaminic pharmaceutical composition comprising ... [DCL] ... ." This reference does not teach the specific combination of DCL and an analgesic.

The Gennaro et al. reference discloses at p. 1131, column 2, numerous binary and ternary pharmaceutical compositions which contain antihistaminic activity and a mild analgesic, "acetaminophen" in particular being specified in the fourth, seventh and eighth compositions listed. Looking elsewhere in the same reference, one finds beginning at p. 1109 an extensive listing of "Analgesics and Antipyretics" with the following compounds listed at the page in parentheses following each name:

i) acetylsalicylic acid (aka aspirin, p. 1110),
ii) acetaminophen (p. 1109),
iii) ibuprofen (p. 1116),
iv) ketoprofen (p. 1112) and
v) naproxen (p. 1118). At p. 1109, column 2, this references states

concerning the complete listing of compounds which follows that "... Most of these agents affect both pain and fever. Consequently they are used widely for minor aches and pains, headaches and the general feeling of malaise that accompanies febrile illness, ..." This reference does not teach the specific combination of DCL and an analgesic.

The teaching of the Villani et al. reference motivates the combination of the antihistamine DCL with other medicinal agents in binary pharmaceutical compositions of the kind specifically embodied at p. 1131 of the Gennaro et al. reference. The substitution of DCL for an antihistamine and the substitution of a different mildly analgesic substance for acetaminophen are therefore deemed to have been variations well within the purview of the ordinary practitioner seeking to optimize the efficacy of the antihistaminic-analgesic binary composition when the antihistamine is DCL. And, while Villani does not specifically teach combinations of DCL with analgesics, the Gennaro reference makes plain by its examples and other teachings that such combinations are notoriously well known and accepted variations in the pharmaceutical composition art, and are widely used to treat mild allergy-related nasal congestion.

Therefore, the instant claimed antihistaminic pharmaceutical compositions comprising DCL and an analgesic selected from the group consisting of acetylsalicylic acid, acetaminophen, ibuprofen, ketoprofen and naproxen would have been obvious to one of ordinary skill in the art having the above cited references before him at the time the invention was made.

(10) New Ground of Rejection.

This Examiner's Answer does not contain any new ground of

rejection.

(11.1) Response to Argument; Anticipation Rejection.

Applicant's arguments filed August 15, 2003 have been fully considered but they are not deemed to be persuasive.

Applicant argues that instant claims **48, 50, 52-53 and 63-65** are not properly anticipated under 35 U.S.C. §102(**b**) because a single reference (**Villani et al. '716**) does not include each and every element of the claimed invention. At page 6 of the Brief, applicant argues specifically that " ... [i]t is clear that Berkow is not being used to interpret the generic disclosure of the '716 patent but instead is an attempt to add a missing element." Examiner respectfully disagrees. Examiner notes that the cited claims in appellant's response are claims wherein DCL is accompanied by a generic "decongestant" only, and the particular decongestant "pseudoephedrine" specified in Berkow et al. is not named. Therefore, on this point the Villani et al. '716 patent standing alone is a proper anticipatory reference. Appellant then argues that the instant '716 patent reference fails because it doe not contain sufficient examples within the range of 0.1 to 5 mg dosage of DCL of specified by the instant claims. Examiner respectfully disagrees and notes that at column 9, Table 1, the dosage of DCL specified at 0.03 mg/kg means a dosage of about 2 mg for a human host weighing 150 pounds (~68 kilograms x 0.03 mg/kg = 2.045 mg dose of active ingredient). In addition, at column 11, lines 30-33, Villani '716 teaches DCL dosages of 10 to 20 mg/day in two to four divided doses, quantities which also clearly fall within the dosage limits of the instant claims. Therefore, the instant '716 patent reference does include examples wherein all of the limitations of the instant claims are met.

In separate arguments limited to claims **54 and 61** appellant argues nearly identically against a finding of anticipation. Examiner therefore refers appellant to the arguments made in response immediately above. With regards to the specific means of administration found in claim **64**, the Villani et al. '716 patent references does not teach this particular route of administration, but Berkow et al. at page 327, end of the paragraph entitled "Treatment," does teach the effectiveness of nasal sprays in the treatment of perennial rhinitis for some hosts.

(11.2) Response to Argument; First Obviousness Rejection.

Applicant's arguments filed August 15, 2003 have been fully considered but they are not deemed to be persuasive.

Appellant asserts, and examiner agrees, that obviousness rejections are properly based on i) a proper motivation to combine references, ii) the prior art must teach or suggest all of the elements of the claims alleged to be obvious, and iii) there must have been a reasonable expectation of success as of the filing date of the instant claims. Appellant also argues against hindsight reconstruction.

Appellant argues that claims **48, 50, 52-53 and 63-65** are not obvious in view of Villani et al. '716 in view of Berkow et al., but by failing to argue lack of motivation or lack of expectation of success, appellant apparently concedes that Villani et al. '716 does provide the proper motivation and showing of expectation of success as specified in the rejection of record. However, appellant does argue that all of the elements of the instant claims are not found in Villani et al. '716. Examiner respectfully disagrees, noting in particular that the '716 reference at column 9, Table 1, the dosage of DCL specified at 0.03 mg/kg means a dosage of about 2 mg for a human host weighing 150

pounds (~68 kilograms x 0.03 mg/kg = 2.045 mg dose of active ingredient). In addition, at column 11, lines 30-33, Villani '716 teaches DCL dosages of 10 to 20 mg/day in two to four divided doses, quantities which also clearly fall within the dosage limits of the instant claims. Therefore, the instant '716 patent reference does include examples wherein all of the limitations of the instant claims are met.

Appellant then argues that Berkow et al. fails to overcome the deficiencies of Villani '716. Examiner notes that Villani discloses DCL, an amount of DCL which lies within the limits of the instant claims, and that this active ingredient may be administered in combination with a "decongestant." Appellant then argues that claims **64 and 65** are not obvious because neither an "elixir" or an aerosol are disclosed by the cited prior art. Examiner respectfully disagrees. With regards to the specific means of administration found in claim **64**, the Villani et al. '716 patent references does not teach this particular route of administration, but Berkow et al. at page 327, end of the paragraph entitled "Treatment," does teach the effectiveness of nasal sprays in the treatment of perennial rhinitis for some hosts. And, the term "elixir" aka "liquid pharmaceutical composition," is also taught in Villani (see column 7, line 30 et seq.) wherein liquid pharmaceutical compositions containing DCL are taught.

Appellant at page 15 of the brief then argues at length that "EVEN WITH THE USE OF HINDSIGHT THE CITED REFERENCES FAIL TO SUGGEST THE CLAIMED INVENTION. (emphasis in original). Appellant cites precedent in support of the view that "when prior art references require selective combination to render obvious a subsequent invention, there must be some reason for the combination other than hindsight." Examiner respectfully disagrees. As clearly noted above and repeated in this response to appellant's arguments, Villani et al. discloses DCL,

amounts of DCL which fall within the claimed range of dosage amount, and a decongestant, and further specify that oral solid and liquid dosage forms are appropriate vehicles for administration. Examiner fails to see where hindsight has occurred.

In separate arguments limited to claims **54 and 61** appellant argues nearly identically against a finding of obviousness. Examiner therefore refers appellant to the arguments made in response immediately above. With regards to the specific means of administration found in claim **64**, the Villani et al. '716 patent references does not teach this particular route of administration, but Berkow et al. at page 327, end of the paragraph entitled "Treatment," does teach the effectiveness of nasal sprays in the treatment of perennial rhinitis for some hosts.

(11.3) Response to Argument; Second Obviousness Rejection.

Applicant's arguments filed August 15, 2003 have been fully considered but they are not deemed to be persuasive.

Appellant argues that Villani et al. '716 discloses an "active compound" (DCL) in optional combination with other therapeutic agents, but that this disclosure is an insufficient basis for combination with Gennaro and the listings of "other therapeutic agent" therein. In particular appellant argues that "Villani provides no disclosure or suggestion of a pharmaceutical composition comprising the *specific* compound DCL, ..." (emphasis as in original). Examiner respectfully disagrees. Applicant is directed to column 9, Table 1 and to claims ***7 and 8*** in Villani et al. '716 wherein specific DCL-containing pharmaceutical compositions are disclosed and claimed. Applicant then argues that Villani does not disclose a pharmaceutical composition

containing DCL and either a non-steroidal anti-inflammatory agent or a non-steroidal analgesic. Examiner agrees that this specific disclosure has not been made and notes that the rejection of record does not so allege. However, when applicant argues that "Villani ... does not even remotely suggest the specific combination of of DCL and a non-steroidal anti-inflammatory agent or a non-steroidal analgesic," examiner respectfully disagrees. Villani plainly teaches pharmaceutical compositions comprising "DCL and other therapeutic agents." Applicant's then argue that only "impermissible hindsight" would permit the combination of the Villani and Gennaro reference, a conclusion with which examiner respectfully disagrees. DCL is plainly an "antihistamine," a fact which would guide the ordinary practitioner to seek disclosures which provide guidance concerning the administration of an "antihistamine" with other "therapeutic agents," the very kind of guidance provided by the Gennaro et al. reference. Therefore, the combination of references has been properly motivated by the type of pharmacological effects generally associated with antihistamine administration in combination with other "therapeutic agents." Applicant then argues that the combination of Villani and Gennaro et al. represents an "obvious to try" situation, implying that the art of binary antihistamine-containing pharmaceutical composition development is unpredictable. Examiner does not know of any teaching in Gennaro et al. or elsewhere to support this point of view, but openly solicits submission of all such relevant teachings which may be known, or may become known, to applicant. And finally, applicant argues that the instant combination of references permits the ordinary practitioner to "impermissibly 'pick and chose'" the DCL of Villani and the analgesics of Gennaro et al. Examiner respectfully disagrees. The term "pick and chose" is an unfair characterization of the instant combination of references, because Gennaro et al. does not have unlimited selection of other "therapeutic agents" which may be

combined with an antihistamine such as DCL.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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